

Please add the following new claims:

c8 5 26. (New) An isolated polymerase encoded by SEQ ID NO:6.

6 27. (New) The isolated polymerase of Claim 26 which has an apparent molecular weight between about 92 000 to 96 000 daltons.

7 28. (New) A stabilized composition comprising a polymerase as claimed in Claim 26 and a stabilizer.

8 29. (New) The composition according to claim 28, wherein said stabilizer is a non-ionic detergent.

9 30. (New) The composition according to Claim 29 wherein dodecylpoly(ethyleneglycolether)_n and/or ethylphenolpoly(ethyleneglycolether)_n serve as a stabilizer.

REMARKS

Claims 1-3, 5-7, 11-13, 15, 16 and 23-25 were pending in the instant application. With the instant Amendment, Claims 1, 2, 11-13, 15, 16 and 23-25 are canceled without prejudice, Claims 3, 5 and 7 are amended and new Claims 26-30 are added. A marked-up version of the amended claims is attached hereto as Exhibit B. Thus, after entry of the instant Amendment, Claims 3, 5-7 and 26-30 are pending and under consideration. For the PTO's convenience, a clean copy of pending Claims 3, 5-7 and 26-30 is attached hereto as Exhibit C.

Applicants expressly reserve the right to pursue any canceled subject matter in one or more related, continuation, divisional or continuation-in-part application(s).

I. THE AMENDMENT OF THE SPECIFICATION

The specification has been amended to correct minor errors in the use of trademarks. As the amendments to the specification are fully supported by the specification as originally filed, they do not constitute new matter. Entry thereof is therefore respectfully requested.

II. THE AMENDMENT OF THE CLAIMS

Claims 1, 2, 11-13, 15, 16 and 23-25 have been canceled without prejudice. Claims 3, 5 and 7 have been amended, and new Claims 26-30 have been added. Claim 3 has been amended to independent form without altering its scope. In particular, the limitations of base Claims 1-2 have merely been incorporated into amended Claim 3. Claim 5 has been amended to depend from Claim 3. Claim 7 has been amended merely to replace trademarks with appropriate generic terminology. The amendment to Claim 7 is supported by the specification, for example, at page 3, lines 26-27.

New Claims 26-30 are fully supported by the specification and claims as originally filed. New Claim 26 recites an isolated polymerase encoded by SEQ ID NO:6. New Claim 26 is supported by the specification and claims as originally filed, for example, at FIG. 3. New Claims 27-30 depend from new Claim 26 and are supported, for example, at FIG. 3 and by original Claims 1-7.

As the amendments to the claims are fully supported by the specification and claims as originally filed, they do not constitute new matter. Entry thereof is therefore respectfully requested.

III. THE COMMENT ON THE SPECIFICATION

The PTO notes that the trademark Thesit should be capitalized and accompanied by generic terminology. With the instant Amendment, Applicants have amended the specification to capitalize the trademark Thesit and to incorporate appropriate generic terminology.

IV. THE OBJECTIONS TO CLAIMS 1 AND 7

Claims 1 and 7 stand objected to because they allegedly recite a misspelled word. Applicants note that Claim 1 has been canceled without prejudice thereby obviating the objection to Claim 1. Applicants also note that amended Claim 7 does not depend from Claim 1 and that amended Claim 7 does not include any misspelled words. Applicants therefore respectfully request that the objections to the claims be withdrawn.

V. THE OBJECTIONS TO CLAIMS 3 AND 7

Claims 3 stands objected to because it depends from rejected Claim 1. With the instant Amendment, Applicants have amended Claim 3 to independent form incorporating the limitations of base Claims 1 and 2 thereby obviating the objection to Claim 3. Applicants therefore respectfully request that the objection to Claim 3 be withdrawn.

Claim 7 stand objected to because it recites a trademark. Applicants have amended Claim 7 replacing the trademark with appropriate generic terminology thereby obviating the objection to the claim. Applicants respectfully request that the objection to Claim 7 be withdrawn.

VI. THE REJECTIONS UNDER 35 U.S.C. § 112

Claims 1, 2 and 5-7 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification. Since Applicants have canceled Claims 1 and 2 with the present Amendment, Applicants submit that the rejections of Claims 1 and 2 are moot and request that they be withdrawn.

Furthermore, Applicants submit that amended Claims 5-7 and new Claims 26-30 are fully described in the specification. 35 U.S.C. § 112, first paragraph, requires that the specification contain a written description of the invention. An applicant must convey with reasonable clarity to those skilled in the art that the applicant was in possession of the invention. *Vas-Cath v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). An adequate description of a chemical genus requires a precise definition by structure, formula, chemical name or physical properties sufficient to distinguish the genus from other materials. *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). The standard for claims involving chemical materials has been explicitly stated by the Federal Circuit:

In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. *Univ. of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

However, description of the function of genetic material is not an adequate description of the genetic material:

In claims to genetic material...a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed

genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. *Id.*

Thus, a claim describing a genus of nucleic acid by structure, formula, chemical name or physical properties sufficient to distinguish the genus from other materials meets the written description requirement of 35 U.S.C. § 112, first paragraph, as elaborated by the Federal Circuit in *Fiers v. Revel* and in *Univ. of California v. Eli Lilly and Co.*

Amended Claims 5-7 depend from Claim 3, which does not stand rejected under 35 U.S.C. § 112. Amended Claims 5-7 recite compositions comprising a purified thermostable DNA polymerase obtainable from *Thermococcus gorgonarius* which catalyzes the template directed polymerization of DNA, possesses 3'-5'-exonuclease (proofreading) activity and is characterized by at least two-fold greater replication fidelity than DNA polymerase obtainable from *Pyrococcus furiosus*, wherein said polymerase retains about 90 % of its activity after incubation for two hours at about 95 °C in the presence of a stabilizer and wherein said polymerase has an apparent molecular weight between about 92 000 to 96 000 daltons. Amended Claims 5-7 thus recite compositions comprising a purified thermostable polymerase by structure or physical properties, for example having a molecular weight between about 92 000 to 96 000 daltons, according to the written description requirement as elaborated in *Fiers v. Revel*. Therefore, amended Claims 5-7 satisfy the requirements for patentability under 35 U.S.C. § 112.

New Claim 26 recites an isolated polymerase encoded by SEQ ID NO:6, and new Claims 27-30 depend from new Claim 26. Claims 26-30 thus recite an isolated polymerase by primary structure according to the written description requirement as elaborated in *Fiers v. Revel*. As such, Claims 26-30 satisfy the written description requirement of 35 U.S.C. § 112.

Applicants respectfully request that the rejections of Claims 5-7 under 35 U.S.C. § 112 be withdrawn. Applicants also submit that new Claims 26-30 satisfy the requirements for patentability under 35 U.S.C. § 112.

CONCLUSION

Applicants submit that Claims 3, 5-7 and 26-30 satisfy all of the criteria for patentability and are in condition for allowance. An early indication of the same and passage of Claims 3, 5-7 and 26-30 to issuance is therefore kindly solicited.

No fees in addition to the extension fee are believed due in connection with this response. However, the Commissioner is authorized to charge all required fees, fees under 37 CFR § 1.17 and all required extension of time fees, or credit any overpayment, to Pennie & Edmonds U.S. Deposit Account No. 16-1150.

Respectfully submitted,

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Enclosure (Exhibits A-C)

EXHIBIT A
MARKED UP VERSIONS OF AMENDED PARAGRAPHS

On page 3, please replace the paragraph beginning "The thermostable DNA..." with the following new paragraph:

--The thermostable DNA polymerase enzyme obtainable from *T. gorgonarius* catalyzes the template directed polymerization of DNA, has an apparent molecular weight of about 92,000 - 96,000 daltons and retains 90 % of its activity after incubation for two hours at 95°C in the presence of a stabilizer like a non-ionic detergent as, e.g., 0.01 % [Thesit™] THESIT™ (Dodecylpoly(ethyleneglycolether)_n) or 0.01 % [Nonidet] NONIDET P40™ (Ethylphenolpoly(ethyleneglycolether)_n).--

On page 5, please replace the paragraph beginning "The DNA polymerase of..." with the following new paragraph:

--The DNA polymerase of the present invention has a very high thermal stability at 95°C. It retains approximately 90 percent of its activity after incubation at 95°C for 120 minutes in the presence of stabilizer. The thermal stability is determined by preincubating the enzyme at the temperature of interest in the presence of all assay components (buffer, MgCl₂, deoxynucleotides, activated DNA and a stabilizer like [0.01 % Thesit™ or 0.01 % Nonidet P40™] 0.01 % THESIT™ (Dodecylpoly(ethyleneglycolether)_n) or 0.01 % NONIDET P40™ (Ethylphenolpoly(ethyleneglycolether)_n)) except the single radioactively-labeled deoxynucleotide. At predetermined time intervals, ranging from 1-120 minutes, small aliquots are removed, and assayed for polymerase activity using one of the methods described above.--

On page 18, please replace the paragraph beginning "The active fractions were...", with the following new paragraph:

--The active fractions were pooled, dialyzed twice against 500 ml Buffer B and applied to a Fractogel TSK AF-Blue column (1x10; 7.8 ml bed volume) equilibrated with buffer B. After washing with 15 ml buffer B, the column was eluted with a linear gradient of 156 ml from 0 to 3 M NaCl in buffer B supplemented with 0.05 % [Thesit] THESIT™ (Dodecylpoly(ethyleneglycolether)_n). The active fractions were pooled and dialyzed against the storage buffer C (20 mM Tris-HCl, pH 8.2; 10 mM 2-mercaptoethanol; 0.1 mM EDTA;

50 mM (NH₄)₂SO₄; 50 % glycerol). After adding of 0.5 % of [Nonidet™ P40] NONIDET P40™ (Ethylphenolpoly(ethyleneglycolether)_n (v/v) and 0.5 % of [Thesit™] THESIT™ (Dodecylpoly(ethyleneglycolether)_n) (v/v) the preparation was stored at -20°C.--

Please replace the paragraph on page 19 beginning "The thermostability of the...", with the following new paragraph:

--The thermostability of the DNA polymerase from *T. gorgonarius* purified as described in Example I was determinated as follows: 5 units purified *T. gorgonarius* polymerase were incubated at 95 °C in 100 µl of the following buffer: 50 mM Tris-HCl, pH 8.8 (at 25 °C); 15 mM (NH₄)₂SO₄; 7 mM MgCl₂; 10 mM 2-mercaptoethanol; 200 µM each of dATP, dGTP, dCTP and dTTP; 0.1% [Nonidet P40] NONIDET P40™ (Ethylphenolpoly(ethyleneglycolether)_n, 0.1% [Thesit] THESIT™ (Dodecylpoly(ethyleneglycolether)_n); 25 µg DNase treated calf thymus DNA. 15 µl samples were taken at 0, 5, 10, 15, 30, 45, 60 and 120 minutes. The remaining polymerase activity was measured as described in example IV by determining incorporation of labeled ³H-TTP into DNA in a 50 µl volume of the incubation mixture described above containing in addition 150 nCi of ³H-TTP. After incubation at 72 °C for 30 minutes the reactions were stopped by addition of 300 µl 10 % TCA, and after 10 minutes at 0 °C the mixtures were applied onto 3MM filters (Whatman). The filters were washed three times with approximately 10 ml 5 % TCA each time, dried for 10 minutes at 75 °C and the DNA bound radioactivity of each filter was measured in 5 ml scintillation liquid in a scintillation vial in LKB rack beta 1217/1218 (Pharmacia).--

EXHIBIT B
MARKED UP VERSIONS OF AMENDED CLAIMS

3. (Twice amended) [The polymerase as claimed in claim 1,] A purified thermostable DNA polymerase obtainable from *Thermococcus gorgonarius* which catalyzes the template directed polymerization of DNA, possesses 3'-5'-exonuclease (proofreading) activity and is characterized by at least two-fold greater replication fidelity than DNA polymerase obtainable from *Pyrococcus furiosus*, wherein said polymerase retains about 90 % of its activity after incubation for two hours at about 95 °C in the presence of a stabilizer and, wherein said polymerase has an apparent molecular weight between about 92 000 to 96 000 daltons.

5. (Twice amended) A stabilized composition comprising a polymerase as claimed in [claim 1] Claim 3 and a stabilizer.

7. (Twice amended) The composition according to Claim 6 wherein [The sit and/or Nonidet P40] dodecylpoly(ethyleneglycolether)_n and/or ethylphenolpoly(ethyleneglycolether)_n serve as a stabilizer.

EXHIBIT C

PENDING CLAIMS AFTER ENTRY OF INSTANT AMENDMENT

3. (Twice amended) A purified thermostable DNA polymerase obtainable from *Thermococcus gorgonarius* which catalyzes the template directed polymerization of DNA, possesses 3'-5'-exonuclease (proofreading) activity and is characterized by at least two-fold greater replication fidelity than DNA polymerase obtainable from *Pyrococcus furiosus*, wherein said polymerase retains about 90 % of its activity after incubation for two hours at about 95°C in the presence of a stabilizer and wherein said polymerase has an apparent molecular weight between about 92 000 to 96 000 daltons.

5. (Twice amended) A stabilized composition comprising a polymerase as claimed in Claim 3 and a stabilizer.

6. The composition according to claim 5, wherein said stabilizer is a non-ionic detergent.

7. (Twice amended) The composition according to Claim 6 wherein dodecylpoly(ethyleneglycolether)_n and/or ethylphenolpoly(ethyleneglycolether)_n serve as a stabilizer.

26. (New) An isolated polymerase encoded by SEQ ID NO:6.

27. (New) The isolated polymerase of Claim 26 which has an apparent molecular weight between about 92 000 to 96 000 daltons.

28. (New) A stabilized composition comprising a polymerase as claimed in Claim 26 and a stabilizer.

29. (New) The composition according to claim 28, wherein said stabilizer is a non-ionic detergent.

30. (New) The composition according to Claim 29 wherein
dodecylpoly(ethyleneglycolether)_n and/or ethylphenolpoly(ethyleneglycolether)_n serve as a
stabilizer.